Caspase-12: Researcher finds new defense mechanism against intestinal inflammation

March 12 2008

The body's first line of defence against pathogenic bacteria that we ingest may not be the immune system but rather the cells that line the intestine. This surprising conclusion is just one facet of a study by Dr. Maya Saleh, a researcher at the Research institute of the McGill University Health Centre that will be published in the journal *Cell Host & Microbe* on March 12.

When pathogenic E. coli bacteria infect the body, they bind to epithelial cells on the interior wall of the intestine before injecting infectious material into the cells with a syringe-like mechanism. This contact triggers a defence reaction within the epithelial cell called the Nod pathway, which results in alerting the immune system as well as in the release of antimicrobial peptides called defensins.

"This mechanism expands our idea of immunity: it hinges upon epithelial cells, not immune cells, early on during infection," says Dr. Saleh. "Furthermore, our study demonstrates that this mechanism is regulated negatively by the Caspase-12 protein, meaning that this protein limits defensin production. This hampers the elimination of bacteria, which then trigger an intense inflammatory reaction manifested by various symptoms including severe diahrrea."

These fundamental discoveries change our understanding of the immune defence. They also open new avenues for a deeper understanding and more targeted treatments of diseases related to intestinal inflammation, such as diarrheal diseases caused by pathogenic E. coli or Crohn's

disease.

In the case of diarrhea, intestinal inflammation is caused by a process similar to the one described above by Dr. Saleh. Treatments that target Caspase-12 would decrease inflammation by acting on the source rather than on the symptoms.

Crohn's disease is the chronic inflammation of the digestive tract, and its specific causes are unknown. What is known, however, is that this pathology is linked to a genetic mutation in the Nod pathway. "This study allows us to consider three possible explanations for Crohn's disease: the Nod pathway mutation could induce either a lack of bacterial "sensing" or a hyperactivation of the immune system resulting in both cases in excessive inflammation against bacteria naturally present in the digestive system; it is also possible that the pathology is caused by an excessive and recurring reaction against a pathogenic microorganism," says Dr. Saleh. The debate is now open.

Source: McGill University